UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/763,836 | 06/08/2001 | Osamu Yamada | 19036/37156 | 3756 |

7590 02/06/2004

Thomas A Cawley Jr
Marshall O'Toole Gerstein Murray & Borun
6300 Sears Tower
233 South Wacker Drive
Chicago, IL 60606-6402

| EXAMINER | |
|---|---|
| SULLIVAN, DANIEL M | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1636 | 22 |

DATE MAILED: 02/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/763,836 | YAMADA ET AL. | |
| | Examiner | Art Unit | |
| | Daniel M Sullivan | 1636 | |

*-- The MAILING DATE f this communication appears on the cover sheet with the correspond nce address --*

**P riod for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *23 June 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *21-24,26,28-31,33-39,44,45 and 47-65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *26,33,34 and 37* is/are allowed.

6)☒ Claim(s) *21-24,28-31,35,36,38,39,44,45,47-53 and 55-65* is/are rejected.

7)☒ Claim(s) *54* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *27 January 2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

This Non-Final Office Action is a reply to the "Amendment in Response to Office Action" of 23 June 2003, filed in response to the Non-Final Office Action mailed 28 January 2003. Claims 21-24, 26, 28-31, 33-39, 44, 45 and 47-56 were considered in the 28 January Office Action. Claims 21, 22-24, 29-31, 44, 45, 47-51 and 56 were amended and claims 57-65 were added in the 23 June Paper. Claims 21-24, 26, 28-31, 33-39, 44, 45 and 47-65 are pending and under consideration.

### *Response to Amendment*

35 U.S.C. § 112, first paragraph, enablement

Rejection of claims 29 and 30 are rejected under 35 U.S.C. 112, first paragraph as lacking enablement for the full scope of the claims is withdrawn in view of the amendment of the claims such that they are now drawn to an isolated host cell and a method of expressing a protein *in vitro*.

Claim Rejections - 35 USC § 112

Rejection of claims 22, 44, 45, 47-51 and 56 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn in view of the amendments of the claims such that the scope of the claimed subject matter is no longer indefinite.

### *New Grounds*

Claim Objections

Claim 54 is objected to because of the following informalities: The word "nucleotide" should be "nucleotides". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-24, 28-31, 35, 36, 38, 39, 44, 45, 47-53 and 55-65 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

In the instant case, the claims are broadly directed to nucleic acids, and methods of using nucleic acids, having the functional property of enhancing protein expression when incorporated

downstream of an expression regulatory promoter sequence and upstream of a protein coding sequence, wherein said nucleic acids are essentially unlimited in structure.

The nucleic acid of claim 21 and claims depending therefrom "comprises a nucleic acid sequence of nucleotides 181-341 of SEQ ID NO: 1 having one thymidine inserted between position 206 and 207 of SEQ ID NO: 1, or a fragment thereof that includes said thymidine". Given the broadest reasonable interpretation of these structural limitation, the nucleic acid of the claims need only comprise at least two consecutive nucleotides comprised within the sequence set forth as SEQ ID NO: 1. That is because the nucleic acid need only comprise "a nucleic acid sequence of the nucleotides..."; therefore any two consecutive nucleotides of the sequence meets the limitation. Further, with regard to a nucleic acid comprising a fragment in including the thymidine, any nucleic acid comprising the sequence ATC meets the structural limitation of the claim. In SEQ ID NO: 1, nucleotide 206 is adenine and nucleotide 207 is cytosine, and insertion of a thymidine results in the fragment of SEQ ID NO: 1, ATC. Therefore, any nucleic acid comprising the fragment ATC reads on the structural limitations of the claim.

The nucleic acid of claim 24, and all claims depending therefrom, is limited to a polynucleotide comprising "a nucleic acid set out in SEQ ID NO: 7". Again, any nucleic acid comprising a two nucleotide stretch of SEQ ID NO: 7 meets this structural limitation because two nucleotides can reasonably be considered a nucleic acid set out in SEQ ID NO: 7.

The nucleic acids of claims 45, 55 and 57, and claims depending therefrom, are similarly directed to polynucleotides comprising "a nucleotide sequence of SEQ ID NO: 7" or "a nucleic acid sequence of nucleotides 181-341 of SEQ ID NO: 1 having one thymidine inserted between position 206 and 207 of SEQ ID NO: 1, or a fragment thereof that includes said thymidine" or

comprising a fragment of SEQ ID NO: 7, which broadly read on any nucleic acid comprising two consecutive nucleotides as set forth in SEQ ID NO: 1 or SEQ ID NO: 7 or comprising the sequence ATC.

Thus, the nucleic acid of the claims encompasses essentially any nucleic acid having the function of enhancing protein expression when incorporated downstream of an expression regulatory promoter sequence and upstream of a protein coding sequence, regardless of the structure of said nucleic acid. An adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself. It is not sufficient to define DNA solely by its principal biological property (i.e., it enhances protein expression) because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any DNA with that biological property. Also, naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, claiming all DNA's that achieve a result without defining what means will do is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). With respect to the method claims, adequate description of the methods first requires an adequate description of the materials, i.e. specific DNA sequences, which provide the means for practicing the invention.

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope because it does not provide adequate written description for

the broad class of nucleic acids encompassed by the claims. Therefore, only the described nucleic acids comprising 181-341 of SEQ ID NO: 1 including one thymidine inserted between position 206 and 207, or SEQ ID NO: 7 meet the written description provision of 35 U.S.C. §112, first paragraph.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 21, 22, 28, 29, 31, 35, 44, 45, 47-49, 51-53 and 57-65 are rejected under 35 U.S.C. 102(b) as being anticipated by Yoo *et al.* (1992) *Virology* 191:889-899 (previously made of record) as evidenced by Brown *et al.* (1992) *Nucleic Acids Res.* 20:5041-5045 (previously made of record).

Yoo *et al.* was originally cited against the claims in the Office Action mailed 10 April 2002 and was subsequently withdrawn in view of amendments to the claims and Applicant's urging that the polynucleotide of the claims is now limited to comprising nucleotides 181-341 of SEQ ID NO: 1 and a thymidine inserted into position 207. However, upon further consideration of the claims, it is apparent that the claims are not so limited (*Id.*). As described above, the claims encompasses essentially any nucleic acid having the function of enhancing protein expression when incorporated downstream of an expression regulatory promoter sequence and upstream of a protein coding sequence, regardless of the structure of said nucleic acid.

Yoo *et al.* teaches an expression vector comprising a nucleic acid sequence of the 5' UTR of hepatitis C virus (page 890, left column, bottom paragraph and page 891, right column, bottom paragraph) enhancement the expression of CAT protein *in vitro* and in cultured mammalian cells (page 892, left column, lines 1-2). In particular, Yoo *et al.* teaches that the nucleotides 1-341 of the 5' UTR were introduced into a vector (page 891, right column, bottom paragraph) and several deletion constructs (see especially Figure 1C and the caption thereto) were used in studying the expression-enhancing ability of the HCV 5' UTR. These constructs meet all of the limitations of the base claims 21 and 45. Further, the isolated polynucleotide of Yoo *et al.* enhances protein expression in an IRES independent manner according to the limitations of independent claim 57 (see especially the section entitled "Translation of hybrid CAT RNAs in poliovirus infected cells" and "Translation of dicistronic mRNA in Huh7 cells" beginning on page 894). In addition, the method of translation of hybrid CAT RNAs *in vivo* set forth in the left and right columns on page 893 meets all of the limitations of the instant method of expressing a protein set forth in claim 30.

The nucleic acid of Yoo *et al.* enhances mRNA translation according to claim 22 (see especially the paragraph bridging pages 892-893); is comprised within an expression vector according to claims 28 and 64; is comprised within an isolated cell according to claims 29; comprises a portion of a coding region taken from a viral gene according to claim 51 and 63 (i.e., the viral ORF shown in Figure 1); is a cDNA according to claim 52; comprises a coding sequence operably inserted downstream of the enhancer according to claim 53. Also, the nucleic acid of Yoo *et al.* is comprised within various mixtures that would meet the limitation of "a composition" according to claims 35 and 65

Further, Brown *et al.* teaches that the 5' UTR of the hepatitis C virus comprises a hairpin structure, which contains a pyrimidine-rich tract, Box A, Box B and a trans factor binding site (see especially Figure 3 and the section entitled "Secondary structure of the 5'NTR of HCV"). Thus, the limitations of dependent claims 44, 47, 48, 58, 59 and 60 are inherent to the nucleic acid. Likewise, the hairpin structure comprised within the nucleic acid of Yoo *et al.* comprises a portion of an IRES according to claim 62. Finally, the sequence disclosed in Brown *et al.* shows that the nucleic acid of Yoo *et al.* also comprises at least one AUG (e.g., at nucleotides 32 to 34) according to claims 49 and 61.

As Yoo *et al.* teaches a nucleic acid, host cell and method comprising all of the limitations of the instant claims, the claimed invention is anticipated by Yoo *et al.*

Claims 21-24, 28-31, 35, 36, 44, 45, 47-50, 53, 55 and 56 are rejected under 35 U.S.C. 102(b) as being anticipated by Collier *et al.* (1998) *J. Gen. Virol.* 79:2359-2366 (previously made of record).

Collier *et al.* was originally cited against the claims in the Office Action mailed 10 April 2002 and was subsequently withdrawn in view of amendments to the claims and Applicant's urging that the polynucleotide of the claims is now limited to comprising nucleotides 181-341 of SEQ ID NO: 1 and a thymidine inserted into position 207. However, upon further consideration of the claims, it is apparent that the claims are not so limited (*Id.*). As described above, the claims encompasses essentially any nucleic acid having the function of enhancing protein expression when incorporated downstream of an expression regulatory promoter sequence and upstream of a protein coding sequence, regardless of the structure of said nucleic acid.

Collier *et al.* teaches a novel bicistronic dual luciferase reporter construct assay system for studying translational efficiencies of 5' UTR form hepatitis C virus, wherein the translation of firefly luciferase is directed by HCV 5' UTR as an IRES (see especially Figure 2, page 2362 and Figure 3, page 2364) *in vivo* and *in vitro.*

The nucleic acids of Collier *et al.* comprise all of the limitations of the base claims 21, 24, 45 and 55, and the method of expressing a luciferase taught by Collier *et al.* meets all of the limitations of claim 30. Further, the nucleic acids of Collier *et al.* increase translation of mRNA by increasing IRES activity according to claims 22, 23 and 50; the vector of Collier is an expression vector which is transfected into a host cell according to claims 28 and 29; the nucleic acid is comprised within various mixtures that would meet the limitation of a composition according to claims 35 and 36; the nucleic acid is a cDNA according to claim 52; and the vector is an eukaryotic expression vector which comprises a protein coding sequence operably inserted downstream of the polynucleotide according to claims 53 and 56.

Finally, in Figure 1, Collier *et al.* teaches the hairpin structure of the HCV 5' UTR which comprises a pyrimidine-rich tract, Box A and Box B (compare to the instant Figure 1) and an AUG (see e.g., nucleotides 32-34) which meets the limitations of claims 44, 47 and 48.

As Collier *et al.* teaches a nucleic acid, host cell and method comprising all of the limitations of the instant claims, the claimed invention is anticipated by Collier *et al.*

***Allowable Subject Matter***

Claims 26, 33, 34 and 37 are allowed.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Friday 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DMS

DAVID GUZO
PRIMARY EXAMINER